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REMARKS

Summary of Personal Interviews with Examiner

Applicants and their attorney thank the Examiner for the courtesy of the telephonic interviews conducted on April 12, 2007 and May 1, 2007 during which the Examiner indicated that the claims presented herein would be allowable.

Amendments to the Claims

Claims 39-53, 57, 59 and 60 were under examination as of the issuance of the Final Office Action. In the Amendment to the Claims spanning pages 2-5 of this paper, claims 39, 40, 41, 47, 48, 50, 51, 53, 57 and 60 have been amended, new claims 61-66 have been added and claims 52 and 59 have been cancelled without prejudice. Accordingly, upon entry of the amendments presented herein, claims 39-51, 53, 57 and 60-66 will remain pending in this application.

Claims 47-53, 57 and 59 were previously withdrawn in response to a Restriction Requirement. Accordingly, it is Applicants' understanding that in view of the Examiner's indication that claims 39 and 60-66 are allowable, claims 47-51, 53 and 57, which are method claims that depend from and include all of the limitations of composition claims 39 and 60-66, should be re-joined in accordance with the provisions of MPEP § 821.04.

Support for the amendments to the claims may be found throughout the specification and in the claims as originally filed. Specifically, claim 60 has been amended and new claims 61-64 have been added merely to re-present markush claim 39 as separate independent claims (claims 39 and 60-64). Accordingly, dependent claims 40, 41 and 57 have been amended as appropriate to correct claim dependencies. Claim 60 has been further amended to indicate that the nucleic acid molecule encodes a polypeptide having a phosphoenolpyruvate carboxykinase activity, support for which can be found throughout the specification, for example, at page 3 of Table 1 of the specification. Support for the amendments to claims 47, 48, 51 and 53 may be found throughout the specification, for example, at page 10, line 1 to page 11, line 34. Finally, support for new claims 65 and 66 may be found throughout the specification, for example, at page 5, lines 11-26.

No new matter has been added by the claim amendments or the introduction of new claims. The amendments to the claims and the cancellation of certain claims should not be construed as an acquiescence to the validity of the Examiner's rejections and were done solely in

the interest of expediting prosecution and allowance of the claims. Applicants reserve the right to pursue the claims as originally filed in one or more further applications.

Priority

Applicants note that certified copies of the foreign German patent applications were submitted with the Response to Final Office Action which was filed on December 4, 2006. Accordingly, Applicants respectfully request that the present application be granted priority to the recited German applications.

Rejection of Claims 39-46 Under 35 U.S.C. § 112, First Paragraph (Enablement)

The Examiner has rejected claims 39-46 under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse the foregoing rejection. In the interest of clarity, Applicants will address each aspect of the Examiner's rejection below.

Rejection of Claims Directed to Sequences of 90% Identity to the Nucleotide Sequence of SEQ ID NO:179

With respect to previously numbered claim 39(c), the Examiner is of the opinion that

> [a]n undue amount of experimentation is required to make the isolated nucleic acid molecule which is at least 90% identical to SEQ ID NO:179 or the complement thereof, where any 195 nucleotides in SEQ ID NO:1 is changed using nucleotide substitution, insertion, deletion, addition, and combinations thereof, and then determining whether the polynucleotide can encode any functional phosphoenolpyruvate carboxykinase. Experimentation also entails searching and screening vast number of biological sources for any naturally occurring allelic variant of SEQ ID NO: 180 and then obtaining the nucleic acid encoding the variant. The specification does not provide guidance, prediction, and working examples for selecting these specific nucleotides to change. Thus, the above stated trail and error experimentation must be performed, which is considered undue experimentation...
>
> ***Amending the claims to recite a nucleic acid molecule comprising a nucleotide sequence which is 95% identical to SEQ ID NO:179 and encodes a polypeptide having phosphoenolpyruvate carboxykinase activity... may overcome the rejection. (Emphasis added).***

Applicants respectfully traverse the foregoing rejection for at least the reasons of record. However, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner's rejection, Applicants have cancelled claim 39(c) and have amended claim 60 in accordance with the Examiner's recommendation, thereby rendering the foregoing rejection moot. Specifically, Applicants have amended claim 60 and have added new claim 61

to be directed to a nucleic acid molecule comprising a nucleotide sequence of at least ***95% or 98% identity***, respectively, to the entire nucleotide sequence of SEQ ID NO:179, wherein the nucleic acid molecule ***encodes a polypeptide having a phosphoenolpyruvate carboxykinase activity***. Similarly, new claims 65 and 66 are directed to a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence which is at least ***95% or 98% identical***, respectively, to the entire amino acid sequence of SEQ ID NO:180, wherein the ***polypeptide has a phosphoenolpyruvate carboxykinase activity***. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 60 (and new claims 61, 65 and 66) and claims depending therefrom.

Rejection of Claims Directed to Nucleotide Sequences of 25 Contiguous Nucleotides

> With regard to previously numbered claim 39(d), the Examiner is of the opinion that experimentation involves selecting any 25 contiguous nucleotides of SEQ ID NO:179 and determining the biological function and use of the selected 25 contiguous nucleotides of SEQ ID NO:179. General teaching regarding screening and searching for the claimed invention using phosphoenolcarboxykinase assays taught in the specification is not guidance for making the claimed invention...
>
> ***[A]mending claim 39 to recite an isolated fragment of at least 25 contiguous nucleotides of SEQ ID NO: 179 may overcome the rejection.*** ***(Emphasis added)***.

Applicants respectfully traverse this rejection for at least the reasons of record. However, solely in the interest of expediting examination and, in no way acquiescing to the validity of the Examiner's rejections, Applicants have re-presented claim 39(d) as new claim 63 directed to a nucleic acid ***fragment that encodes a polypeptide having a phosphoenolpyruvate carboxykinase activity***. This amendment was made in accordance with the Examiner's recommendations and, accordingly, Applicants respectfully submit that this amendment is sufficient to render the Examiner's rejection moot.

Notwithstanding the foregoing, Applicants wish to make the following remarks of record. Applicants respectfully submit that, based on the teachings in the specification and the general knowledge in the art at the time of the invention, one skilled in the art would be able to make and use a nucleic acid molecule comprising a nucleotide sequence of at least 25 contiguous nucleotides of SEQ ID NO: 179 and having a phosphoenolpyruvate carboxykinase activity. As provided in the previous response, the present specification contains ample guidance on how to make and use such fragments, for example, using standard synthetic

techniques such as an automated DNA synthesizer (see, for example, page 23, lines 12-37 of the specification) or using chemical synthesis and enzymatic ligation reactions (see, for example, page 31, lines 24-26). Moreover, standard techniques well known by a skilled artisan, for example, the use of restriction enzymes to cleave at specific sites of a DNA sequence, could also be used for generating such fragments. In addition, as taught in the specification, for example, at page 26, line 33 to page 27, line 10, nucleic acid fragments that encode biologically active portions of the polypeptides of the invention can be designed by incorporating an active domain known to be important for phosphoenolpyruvate carboxykinase activity. For example, as set forth in the previous response, the domain [F/Y]-P-S-[A/G/M/S]-C-G-K-T-[N/S] (amino acid residues 270-278 of SEQ ID NO:2 encoded by nucleotide residues 908-934 of SEQ ID NO:1) had been identified at the time of filing of the present application as a highly conserved phosphoenolpyruvate carboxykinase domain that is involved in enzymatic activity (see PROSITE entry for PEPCK_GTP, attached herein as Appendix A; see also Lewis *et al.* "Cysteine 288: An Essential Hyperreactive Thiol of Cytosolic Phosphoenolpyruvate Carboxykinase (GTP)" (1989) *J. Biol. Chem.* 264(1):27-33), attached herein as Appendix B). As described by Lewis *et al.*, the cysteine residue, in particular, at the center of the aforementioned domain was known to be essential to the catalytic properties of phosphoenolpyruvate carboxykinase. Moreover, the specification, for example, at Example 8, at page 56, lines 1-28 of the specification, provides assays for confirming that such fragments of at least 25 contiguous nucleotides retain a phosphoenolpyruvate carboxykinase activity. Based on the foregoing teachings in the specification and the general knowledge in the art at the time of the invention, one skilled in the art would be able to make and use the claimed nucleic acid molecules using only routine experimentation.

New claim 64 has also been added in accordance with the Examiner's recommendations. Specifically, new claim 64 is directed to a nucleic acid molecule ***consisting of*** a fragment of at least 25 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:179. During the telephonic interview of November 29, 2006, the Examiner had indicated that such claim, being directed to, for example, fragments of at least 25, 30, 50 or 75 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:179 (without any heterologous 3' or 5' nucleotide sequences) is in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph.

For each of the foregoing reasons, Applicants respectfully submit that one skilled in the art would be able to make and use the nucleic acid molecules of the present invention using only routine experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. § 112, first paragraph for lack of enablement.

Rejection of Claims 39-46 Under 35 U.S.C. § 112, First Paragraph (Written Description)

The Examiner has also rejected claims 39-46 and 60 under 35 U.S.C. § 112, first paragraph as allegedly "failing to comply with the written description requirement." In particular, the Examiner is of the opinion that

> [c]laim 39 is drawn to a genus of nucleic acid molecules comprising any fragment of at least 25 contiguous nucleotides of SEQ ID NO:179. Claim 60 is drawn to a genus of nucleic acid molecules comprising a nucleotide sequence which is at least 95% identical to SEQ ID NO:179. The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing nucleotide sequences. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exist...
>
> While the specification discloses a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:179 which encodes a phosphoenolpyruvate carboxykinase from *Corynebacterium glutamicum* consisting of the amino acid sequence of SEQ ID NO: 180; there is no recitation of any particular structure to function relationship in the claims which would define any biological properties and enzyme activities common to the members of each genus. Furthermore, the specification does not define any structure to function relationship for each claimed genus other than the polynucleotide of SEQ ID NO:179 encoding a phosphoenolpyruvate carboxykinase consisting of the amino acid sequence of SEQ ID NO: 180. Thus one skilled in the art cannot visualize or recognize the identity of the members of the genus...
>
> ***Amending the claims to recite a nucleic acid molecule comprising a nucleotide sequence which is 95% identical to SEQ ID NO: 179 and encodes a polypeptide having phosphoenolpyruvate carboxykinase activity, and further amending claim 39 to recite an isolated fragment consisting of at least 25 contiguous nucleotides of SEQ ID NO:179 may overcome the rejection. (Emphasis added).***

Applicants respectfully traverse this rejection on the grounds that, based on the teachings in Applicants' specification and the general knowledge in the art at the time of the invention, one skilled in the art would reasonably conclude that the Applicants were in possession of the

claimed invention at the time the application was filed. In the interest of clarity, Applicants will address each aspect of this rejection below.

Rejection of Claims Directed to Sequences of 90% Identity to the Nucleotide Sequence of SEQ ID NO:179

With regard to the Examiner's rejection of previously numbered claim 39(c) and claim 60, Applicants respectfully traverse this rejection for at least the reasons of record. However, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner's rejection, Applicants have cancelled claim 39(c) and have amended claim 60 in accordance with the Examiner's recommendations, thereby rendering the foregoing rejection moot. Specifically, Applicants have amended claim 60 and have added new claim 61 to be directed to a nucleic acid molecule comprising a nucleotide sequence of at least ***95% or 98% identity, respectively,*** to the entire nucleotide sequence of SEQ ID NO:179, wherein the nucleic acid molecule ***encodes a polypeptide having a phosphoenolpyruvate carboxykinase activity.*** Similarly, new claims 65 and 66 are directed to a nucleic acid molecule encoding a polypeptide comprising an amino acid sequence which is at least ***95% or 98% identical,*** respectively, to the entire amino acid sequence of SEQ ID NO:180, wherein the ***polypeptide has a phosphoenolpyruvate carboxykinase activity.*** Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 60 (and new claims 61, 65 and 66) and claims depending therefrom.

Rejection of Claims Directed to Nucleotide Sequences of 25 Contiguous Nucleotides

With respect to the Examiner's rejection of previously pending claim 39(d), currently pending as new claim 63, Applicants respectfully traverse the foregoing rejection for at least the reasons of record. However, solely in the interest of expediting examination and in no way acquiescing to the validity of the Examiner's rejection, Applicants have re-presented claim 39(d) as new claim 63 directed to a nucleic acid fragment that ***encodes a polypeptide having a phosphoenolpyruvate carboxykinase activity.*** This amendment was made in accordance with the Examiner's recommendations and, accordingly, Applicants respectfully submit that this amendment is sufficient to render the Examiner's rejection moot.

Notwithstanding the foregoing, Applicants wish to make the following remarks of record. Applicants respectfully submit that the present specification provides teachings sufficient to demonstrate that Applicants were in possession, at the time of filing, of the genus of fragments of at least 25 contiguous nucleotides of SEQ ID NO:179 which encode polypeptides exhibiting a phosphoenolpyruvate carboxykinase activity. As set forth in the previous response, Applicants teach, for example, at page 26, line 33 to page 27, line 5 of the specification, that such fragments could be designed by the incorporation of active domains of the phosphoenolpyruvate carboxykinase protein that participate in the metabolism of carbon compounds such as sugars, or in energy-generating pathways. As previously submitted, such domains were well known in the art at the time of the filing of the present application. For example, as set forth above, the domain [F/Y]-P-S-[A/G/M/S]-C-G-K-T-[N/S] (amino acid residues 270-278 of SEQ ID NO:180 encoded by nucleotide residues 908-934 of SEQ ID NO:179) had been identified at the time of filing of the present application as a highly conserved domain among phosphoenolpyruvate carboxykinase proteins. Moreover, Example 8, at page 56, lines 1-28 of the specification, in addition to standard techniques known in the art at the time of the filing of the present application, provides means of identifying those fragments of at least 25 contiguous nucleotides which retain a phosphoenolpyruvate carboxykinase activity.

Applicants further submit that claim 63, as pending, is defined both structurally and functionally. Indeed, the claimed fragments are defined structurally, *i.e.*, a sequence of at least 25 contiguous nucleotides of SEQ ID NO:179, and functionally, *i.e.*, encoding a polypeptide having a phosphoenolpyruvate carboxykinase activity. Accordingly, Applicants submit that sequences of at least 25 contiguous nucleotides of SEQ ID NO:179 that encode polypeptides having a phosphoenolpyruvate carboxykinase activity are sufficiently described to demonstrate to a skilled artisan that Applicants were in possession of the claimed sequences at the time of filing.

New claim 64 has been added in accordance with the Examiner's recommendations. Specifically, new claim 64 is directed to a nucleic acid molecule ***consisting of*** a fragment of at least 25 contiguous nucleotides of the nucleotide sequence of SEQ ID NO:179. During the telephonic interview of November 29, 2006, the Examiner indicated that such claim is in compliance with the written description requirement of 35 U.S.C. §112, first paragraph.

In view of each of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims under 35 U.S.C. §112, first paragraph, as lacking written description.

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Application No.: 10/781014 Docket No.: BGI-126CPCN

CONCLUSION

In view of the foregoing remarks, allowance of all pending claims is respectfully requested. If there are any remaining issues or if the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

The Commissioner is hereby authorized to charge any deficiency in the fees paid herewith, or credit any overpayment, to Deposit Account No. 12-0080, under Order No. BGI-126CPCN, from which the undersigned is authorized to withdraw.

Dated: **May 1, 2007**

Respectfully submitted,

By _____

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